

## PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :  C07K 14/00, 14/705		A3	(11) International Publication Number: <b>WO 00/26243</b>  (43) International Publication Date: 11 May 2000 (11.05.00)
<p>(21) International Application Number: PCT/US99/25499</p> <p>(22) International Filing Date: 29 October 1999 (29.10.99)</p> <p>(30) Priority Data: 60/172,249 29 October 1998 (29.10.98) US</p> <p>(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 60/172,249 (CIP) Filed on 29 October 1998 (29.10.98)</p> <p>(71) Applicant (for all designated States except US): INCYTE PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95033 (US). ARGENTINE, Charles, C. [US/US]; 1849 8th Avenue, Unit B, Alameda, CA 94510 (US). CORLEY, Neil, C. [US/US]; 1240 Dale Avenue, #30, Mountain View, CA 94040 (US). GORGONE, Gina, A. [US/US]; 1253 Pinecrest Drive, Boulder Creek, CA 94132 (US). GUEGLER, Karl, J. [CH/US]; 1048 Oakland Avenue, Menlo Park, CA 94025 (US).</p>		<p>BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US).</p> <p>(74) Agents: BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US).</p> <p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p> <p>(88) Date of publication of the international search report: 5 October 2000 (05.10.00)</p>	
<p>(54) Title: TRANSMEMBRANE 4 PROTEINS</p> <p>(57) Abstract</p> <p>The invention provides human transmembrane 4 proteins (TM4P) and polynucleotides which identify and encode TM4P. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of TM4P.</p>			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/25499

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C07K14/00 C07K14/705

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>YUASA T. ET AL.: "Expression of uroplakin Ib and uroplakin III genes in tissues and peripheral blood of patients with transitional cell carcinoma" JAPANESE JOURNAL OF CANCER RESEARCH, vol. 89, September 1998 (1998-09), pages 879-882, XP000882554 abstract page 879, column 1, line 1 -page 881, column 1, paragraph 1; figure 1 ---</p> <p style="text-align: center;">-/-</p>	1-16,19

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

6 April 2000

07.07.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Muller-Thomalla, K

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/25499

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL SEQUENCE DATABASE [Online] EMBL, Heidelberg Accession number: P30413, 1 April 1993 (1993-04-01) KALLIN ET AL.: "Cloning of a growth arrest-specific and transforming growth factor beta-regulated gene, TI 1, from an epithelial cell line" XP002134989 abstract ---	1-16,19
X	DATABASE EMBL SEQUENCE DATABASE [Online] EMBL, Heidelberg Accession number: P38573, 1 October 1994 (1994-10-01) YU ET AL.: "Uroplakins Ia and Ib, two major differentiation products of bladder epithelium, belong to a family of four transmembrane domain (4TM) proteins" XP002134990 abstract ---	1-16,19
A	WRIGHT M D ET AL: "The ins and outs of the transmembrane 4 superfamily" IMMUNOLOGY TODAY, GB, ELSEVIER PUBLICATIONS, CAMBRIDGE, vol. 15, no. 12, 1 January 1994 (1994-01-01), pages 588-594, XP002066879 ISSN: 0167-5699 the whole document ---	1-16,19
P,X	WO 99 00408 A (INCYTE PHARMA INC ;CORLEY NEIL C (US); SHAH PURVI (US); HILLMAN JE) 7 January 1999 (1999-01-07) the whole document -----	1-16,19

# INTERNATIONAL SEARCH REPORT

I. International application No.  
PCT/US 99/25499

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
Although claim 19 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2.  Claims Nos.: 17, 18, 20 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210

3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1 (partly) - 16 (partly) and 19 (partly)

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box I.2

Claims Nos.: 17,18,20

Present claims 17,18 and 20 relate to a compound and method using the same defined by reference to a desirable characteristic or property, namely an agonist or antagonist effect with respect to the polypeptide of claim 1.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has not been carried out for those claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1(partly)-16(partly) and 19(partly)

A purified polypeptide comprising an amino acid sequence as shown in sequence No: 1 and the corresponding encoding polynucleotide comprising an nucleic acid sequence as shown in sequence No:3. Expression vectors comprising the polynucleotide and host cell comprising the expression vector as well as methods for detecting the polynucleotide. Polynucleotide which hybridizes or is complementary to the encoding polynucleotide as shown in sequence No: 3. Method for producing the polypeptide and an antibody which specifically binds to the latter. A pharmaceutical composition comprising the polypeptide and method of treatment using the same.

2. Claims: 1(partly)-16(partly) and 19(partly)

A purified polypeptide comprising an amino acid sequence as shown in sequence No: 2 and the corresponding encoding polynucleotide comprising an nucleic acid sequence as shown in sequence No:4. Expression vectors comprising the polynucleotide and host cell comprising the expression vector as well as methods for detecting the polynucleotide. Polynucleotide which hybridizes or is complementary to the encoding polynucleotide as shown in sequence No: 4. Method for producing the polypeptide and an antibody which specifically binds to the latter. A pharmaceutical composition comprising the polypeptide and method of treatment using the same.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 99/25499

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9900408	A 07-01-1999	AU 7572398 A	19-01-1999